

WHAT IS CLAIMED IS:

1                   1.       A composition for the treatment of an anorectal disorder, and for  
2       controlling the pain associated therewith, said composition comprising a NO donor in  
3       admixture with a second agent selected from the group consisting of phosphodiesterase  
4       type II inhibitors, phosphodiesterase type IV inhibitors, phosphodiesterase type V  
5       inhibitors, nonspecific phosphodiesterase inhibitors, superoxide scavengers,  $\beta$ -adrenergic  
6       agonists, cAMP-dependent protein kinase activators,  $\alpha_1$ -adrenergic antagonists, estrogens,  
7       ATP-sensitive  $K^+$  channel activators and smooth muscle relaxants, with a  
8       pharmaceutically acceptable carrier.

1                   2.       A composition in accordance with claim 1, wherein said NO donor  
2       is selected from the group consisting of nitroglycerin, L-arginine, SNAP, GSNO and SIN-  
3       1, and said second agent is a superoxide scavenger selected from the group consisting of  
4       superoxide dismutase and chemical superoxide dismutase mimetics.

1                   3.       A composition in accordance with claim 1, wherein said carrier is  
2       formulated for local application.

1                   4.       A composition in accordance with claim 1, wherein said second  
2       agent is selected from the group consisting of phosphodiesterase type II inhibitors,  
3       phosphodiesterase type IV inhibitors, phosphodiesterase type V inhibitors, and  
4       nonspecific phosphodiesterase inhibitors.

1                   5.       A composition in accordance with claim 1, wherein said second  
2       agent is selected from the group consisting of  $\beta$ -adrenergic agonists.

1                   6.       A composition in accordance with claim 5, wherein said  $\beta$ -  
2       adrenergic agonist is selected from the group consisting of  $\beta_2$ -adrenergic agonists and  
3        $\beta_3$ -adrenergic agonists.

1                   7.       A composition in accordance with claim 1, wherein said second  
2       agent is selected from the group consisting of ATP-sensitive  $K^+$  channel activators.

1                   8.       A composition for the treatment of an anorectal disorder, and for  
2       controlling the pain associated therewith, said composition comprising a  
3       phosphodiesterase inhibitor and a pharmaceutically acceptable carrier.

1                   9.     A composition in accordance with claim 8, wherein said  
2 phosphodiesterase inhibitor is selected from the group consisting of phosphodiesterase  
3 type II inhibitors, phosphodiesterase type IV inhibitors, phosphodiesterase type V  
4 inhibitors, and nonspecific phosphodiesterase inhibitors.

1                   10.    A composition in accordance with claim 9, further comprising an  
2 agent selected from the group consisting of  $\beta$ -adrenergic agonists, cAMP-dependent  
3 protein kinase activators,  $\alpha_1$ -adrenergic antagonists, L-type  $\text{Ca}^{2+}$  channel blockers,  
4 estrogens, ATP-sensitive  $\text{K}^+$  channel activators and smooth muscle relaxants.

1                   11.    A composition for the treatment of an anorectal disorder, and for  
2 controlling the pain associated therewith, said composition comprising a  $\beta$ -adrenergic  
3 agonist and a pharmaceutically acceptable carrier.

1                   12.    A composition in accordance with claim 11, wherein said  $\beta$ -  
2 adrenergic agonist is specific for a receptor isoform selected from the group consisting of  
3  $\beta_2$ ,  $\beta_3$  and combinations thereof.

1                   13.    A composition in accordance with claim 11, wherein said  $\beta$ -  
2 adrenergic agonist is isoproterenol.

1                   14.    A composition in accordance with claim 11, further comprising an  
2 agent selected from the group consisting of cAMP-hydrolyzing PDE inhibitors,  
3 nonspecific PDE inhibitors,  $\alpha_1$ -adrenergic antagonists, estrogens, L-type  $\text{Ca}^{2+}$  channel  
4 blockers, ATP-sensitive  $\text{K}^+$  channel activators and smooth muscle relaxants.

1                   15.    A composition for the treatment of an anorectal disorder, and for  
2 controlling the pain associated therewith, said composition comprising an ATP-sensitive  
3  $\text{K}^+$  channel activator and a pharmaceutically acceptable carrier.

1                   16.    A composition in accordance with claim 15, further comprising an  
2 agent selected from the group consisting of cAMP-dependent protein kinase activators,  
3 estrogens,  $\alpha_1$ -adrenergic antagonists, L-type  $\text{Ca}^{2+}$  channel blockers and smooth muscle  
4 relaxants.

1                   17.     A composition for the treatment of an anorectal disorder, and for  
2     controlling the pain associated therewith, said composition comprising an  $\alpha_1$ -adrenergic  
3     antagonist and a pharmaceutically acceptable carrier.

1                   18.     A composition in accordance with claim 17, said composition  
2     further comprising an agent selected from the group consisting of cAMP-hydrolyzing  
3     phosphodiesterase inhibitors, estrogens and smooth muscle relaxants.

1                   19.     A composition in accordance with claim 17, wherein said cAMP-  
2     hydrolyzing phosphodiesterase inhibitor is a phosphodiesterase type IV inhibitor.

1                   20.     A composition for the treatment of an anorectal disorder, and for  
2     controlling the pain associated therewith said composition comprising a cAMP-dependent  
3     protein kinase activator and an L-type  $\text{Ca}^{2+}$  channel blocker.

1                   21.     A composition for the treatment of an anorectal disorder, and for  
2     controlling the pain associated therewith, said composition comprising a cGMP-  
3     dependent protein kinase activator and a pharmaceutically acceptable carrier..

1                   22.     A composition for the treatment of an anorectal disorder, and for  
2     controlling the pain associated therewith, said composition comprising a nonspecific  
3     cyclic nucleotide-dependent protein kinase activator, optionally in admixture with a  
4     smooth muscle relaxant.

1                   23.     A method of treating an anorectal disorder, and for controlling the  
2     pain associated therewith, the method comprising administering to a subject in need of  
3     such treatment a therapeutically effective amounts of a NO donor and a second agent  
4     selected from the group consisting of phosphodiesterase type II inhibitors,  
5     phosphodiesterase type IV inhibitors, phosphodiesterase type V inhibitors, nonspecific  
6     phosphodiesterase inhibitors, superoxide scavengers,  $\beta$ -adrenergic agonists, cAMP-  
7     dependent protein kinase activators,  $\alpha_1$ -adrenergic antagonists, estrogens, L-type  $\text{Ca}^{2+}$   
8     channel blockers, ATP-sensitive  $\text{K}^+$  channel activators and smooth muscle relaxants.

1                   24.     A method in accordance with claim 23, wherein said NO donor and  
2     said second agent are administered in combination.

1                   25.     A method in accordance with claim 23, wherein said second agent  
2     is administered prior to said NO donor.

1                   26.     A method in accordance with claim 23, wherein said anorectal  
2     disorder is an anal fissure.

1                   27.     A method of treating an anorectal disorder, and for controlling the  
2     pain associated therewith, the method comprising administering to a subject in need of  
3     such treatment a therapeutically effective amount of a composition comprising a  
4     phosphodiesterase inhibitor.

1                   28.     A method in accordance with claim 27, further comprising  
2     administering to said subject a second agent selected from the group consisting of  $\beta$ -  
3     adrenergic agonists, cAMP-dependent protein kinase activators,  $\alpha_1$ -adrenergic  
4     antagonists, estrogens, L-type  $\text{Ca}^{2+}$  channel blockers, ATP-sensitive  $\text{K}^+$  channel activators  
5     and smooth muscle relaxants.

1                   29.     A method of treating an anorectal disorder, and for controlling the  
2     pain associated therewith, the method comprising administering to a subject in need of  
3     such treatment a therapeutically effective amount of a composition comprising a  $\beta$ -  
4     adrenergic agonist.

1                   30.     A method in accordance with claim 29, further comprising  
2     administering to said subject a second agent selected from the group consisting of cAMP-  
3     dependent protein kinase activators,  $\alpha_1$ -adrenergic antagonists, estrogens, L-type  $\text{Ca}^{2+}$   
4     channel blockers, ATP-sensitive  $\text{K}^+$  channel activators and smooth muscle relaxants.

1                   31.     A method of treating an anorectal disorder, and for controlling the  
2     pain associated therewith, the method comprising administering to a subject in need of  
3     such treatment a therapeutically effective amount of a composition comprising an ATP-  
4     sensitive potassium channel opener and an agent that promotes cAMP-mediated anal  
5     sphincter relaxation.

1                   32.     A method of treating an anorectal disorder, and for controlling the  
2     pain associated therewith, the method comprising administering to a subject in need of  
3     such treatment a therapeutically effective amount of a composition comprising a

4 . potassium channel opener, wherein said therapeutically effective amount decreases  
5 hypertonicity of an anal sphincter muscle of the subject.

1                   33.     A method of treating an anorectal disorder, and for controlling the  
2 pain associated therewith, the method comprising administering to a subject in need of  
3 such treatment a therapeutically effective amount of a composition comprising a  
4 pharmaceutically acceptable carrier and an agent which increases a level of cyclic  
5 guanidine monophosphate or cyclic adenosine monophosphate in a tissue of an anal  
6 sphincter muscle of the subject, thereby decreasing hypertonicity of the anal sphincter  
7 muscle of the subject.

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